

**Remarks**

Claims 1-3 and 13 are pending in this application.

Claims 4-9 and 11-12 have been cancelled by this Amendment. Claim 10 was previously cancelled. New Claim 13 has been added in this Amendment.

Claim 13 is supported at least by previous claims 4 and 5 and page 19, first paragraph of the specification in this case. Applicants respectfully contend no new matter is added by this new claim and the claim is fully supported by the disclosure.

Although Applicants disagree with the Examiner's position on enablement, in order to expedite prosecution, Claims 6-9 and 11-12 have been cancelled. Claims 4 and 5, relating to compositions, have been cancelled and new Claim 13 presented. As a result, paragraphs 3-12 of the July 20, 2006 Office Action are no longer applicable.

Claims 1-3 stand rejected under 35 U.S.C. 103(a) as obvious over Mitch, et al., compound 11 in view of Armer, et al, EP 1072592, pages 2-5. Applicants respectfully traverse the rejection and request reconsideration.

Applicants respectfully contend a combination of the two references does not establish a prima facie case of obviousness for the presently claimed compound. Further, even if the combination of the two references is deemed to establish a prima facie case of obviousness, data in the specification effectively rebuts such prima facie obviousness.

Armer, et al. (EP 1072592) at page 2, paragraph 0006, acknowledges the Mitch, et al. J. Med. Chem. journal article as prior art to it. As the skilled artisan reviews the preferences of substituents disclosed in EP 1072592, it quickly becomes apparent that the 1-piperidine substituent comprising a 3-hydroxy-3-cyclohexylpropyl group is not included within those preferences (see page 4, paragraphs 0017 and 0018 and page 5, paragraph 0019). Clearly, the skilled artisan would appreciate the amido group at the three position of the phenyl ring affords activity only with alternative 1-piperidine substituents. The clearly stated prior knowledge of the Mitch, et al., J. Med. Chem. reference by Armer, et al. requires this conclusion. As such, when the two references are viewed in combination, the skilled artisan is led away from picking and choosing substituents and recombining them in the fashion the Examiner has done in the July 20, 2006 Office Action. Applicants respectfully contend a combination of the two references, when viewed from the position of one skilled in the art, does not establish a prima facie case of obviousness.

The Mitch, et al., J. Med. Chem. Article, compound 11, that has been particularly

identified by the Examiner is also disclosed, and claimed, in US Patent 4,891,379 which is identified in several places in the disclosure of the present application and is cited relevant art.

Assuming solely for purposes of further discussion, the Examiner deems a prima facie case of obviousness is established by the combination of the two references, Applicants respectfully direct the Examiner's attention to Table 1 on page 16 of the present disclosure; Table 2 on page 17 of the present disclosure; and Table 3 on page 18 of the present disclosure. As stated in the disclosure at page 16, beginning at line 3, the compound of the present invention is "at least 2 fold more potent than the compound of formula (II)..." exemplified as example 2 in the Armor, et al. EP reference and demonstrates comparable potency compared to compound (III) which is disclosed and claimed in US Patent No. 4,891,379 and is also example 11 of the Mitch, et al. journal article. Table I is, of course, a summary of in vitro activity.

Table 2 provides data showing that the compound of the present invention demonstrates better bioavailability than compound 11 of the Mitch, et al. journal article. Higher numbers in Table 2 evidence enhanced bioavailability.

Also as stated on page 17, the compound of the present invention exhibits "a significantly reduced potential for inhibiting the cytochrome P450 enzyme system." This is further stated to be a surprising and unexpected finding that affords improved safety and reduced potential for drug-drug interactions. This characteristic of the compound of the present invention was discovered using a standard assay that monitors a compound's ability to inhibit Cyp2D6, a member of the cytochrome P450 family of enzymes. As shown in Table 3 on page 18 of the disclosure, the compound of the present invention (formula 1) is about 16 times less likely to cause inhibition of the cytochrome P450 enzyme compared to compound 11 of the Mitch, et al. reference. Further, the data in Table 3 shows the compound of the present invention is more than 4 times less likely to inhibit the cytochrome P450 enzyme system compared to example 2 of the Armer, et al. EP reference.

Applicants respectfully contend the data in Tables 1, 2 and 3 clearly rebuts any prima facie case of obviousness that may be deemed to exist through a combination of the two cited references.

Applicants respectfully contend a prima facie case of obviousness has not been established by a combination of the two references identified by the Examiner. Further, Applicants contend that even if a prima facie case of obviousness is deemed to exist, data in the specification has effectively rebutted such prima facie case of obviousness.

Applicants respectfully request favorable reconsideration of the invention as presently claimed and in view of the remarks presented in this paper.

Respectfully Submitted,

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